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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

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04/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	09/423,698	LEROY, ODILE	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 April 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645

Applicants arguments have been carefully considered but are not persuasive. Applicants argue that varying the ration of carbohydrate to preotein would not lead the skilled artisan to the invention which for the first time provides for the combination of DT and TT carriers. This is not persuasive because the rejection is over a combination of references and the combination also provides for the combination of DT and TT. Applicants aruge that Klein et al does not teach how the ratio of carbohydrate to carrier protein influnces immunogenicity and therefore does not direct one skilled in the art to routine basis of vaccine formulation. This is not persuasive, the variables in vaccination were known to the art, it is routine in this to optimize known variables. That the experimentaion would be extensive does not make it undue or provide for a lack of expectation of success, especially in view of the fact that several vaccine conjugates of polysaccharide and pneumonococcal polysaccharide in particular were known to the art and sucessful at providing for vaccination. Applicants argue that the factors that Klien et al lists results in the manufacture and rendering of vaccines a priori unpredicatable. This is not persuasive, the variables were known to the art. Further, if the art was so unpredicatable why have several conjugate vaccines been produced and clearly Applicants claims are not commensurate in scope with their asserted highly unpredictable art. In the pneumonococcal arts, there exists multiple sucessful vaccines. The 23-way vaccine, the 7-way conjugate, and various other conjugates in phase 1-3 trials. As such, in this field there have been multiple successes for unconjugated and conjugated vaccines in the prior art of record. Applicants argue that Klein et al teach that the art is unpredicatable and the application of the HIb conjugae to the improvement of the existing penumonococcal vaccine may be difficult. This is not persuasive because the art of record at the time the invention was made did provide for a reasonable expectation of success and Klein et al teaches that practical limits indicate that the conjugate vaccine have less than the 23 carbohydrates. It is noted that the Klein et al directs the skilled artisan to less than 23-way vaccine, but does not teach that such would not be effective to provide for immunization, but indicates that there is doubt to improvement of the 23-way vaccine when read in context. It is noted that the art provides for multiple successes with combinations of carriers and that the art directs one to the conjugation and that it was effective for immunizaiton. Applicants argue that Klein et al is not alone in these teachings and that the problem of carrier suppression is known to the art with known carrier proteins and the art recognized the solution of using multiple carriers in combination vaccines to get over this effect. This is not persuasive, the problem was clearly known and the solution was to use multiple carriers. The claims are not limited to Dt and Tt carriers but the combination of different carriers where Dt and Tt are two of the carriers. Applicants ignore that the solution of combining carriers in mixed vaccines was a known solution to the carrier suppression. That is one used multiple carriers in order to prevent the effect. Applicants would have one believe that Dt and Tt are the only components of the vaccine. This is not persuasive because the composition comprises and the use of multiple different carrier proteins was known. Further, Applicants arguments that the "wisdom in the art" was to avoid Dt and Tt files in the face of the sucessful vaccine of Ahman et al at the time of the invention. Applicants invention is NOT limited to the combination of Dt and Tt carrier proteins. They are two of many that could be present in a combination vaccine. Applicants also argue deVelasco et al that warn against carrier suppression with a single carrier protein. This is again not persuasive, the art as combined teaches combination of different carriers and the composition per se is not limited to the argued Dt and Tt carriers. Applicants argue that if Klein et al intended to refere to multiple carriers in a single vaccine, the skilled artisan would have expected a more detailed discussion This is not persuasive because it is pure speculation on the part of Applicants. Applicants argue that the study at page 4 of the specificaiton with the addition of excess unconjugated Dt and Tt are of concern here and would direct one skilled in the art to using Dt and Tt. This is again not persuaisve all that this indicates is that excess unconjugated Dt and Tt are a potential problem and that the skilled artisan would not combine with FREE Dt and Tt vaccines. Applicants argue that the only examples of multiple carrier proteins and multiple serotype are post-filing. This is simply not true for carriers in genera and saccharides in general and Applicants are directed to the combination of carriers and saccharides in general. Applicants would have one believe that they were the first to combine different carriers and different saccharides. This is simply not so, while they may be the first to combine Dt and Tt pneumonococcal conjugates, the art of record clearly indicates that they were not the first to combine different carriers and different polysaccharides in the same vaccine formulation. Applicants argue that the obvious to try standard of KSR is not relevant here because the solutions are not finite, predictable and known. This is not persuasive because the polysaccharides and carriers were known, there is direction and guidance in the art to choose different ones. Applicants argue that the success of the 23-valent vaccine is not relevant or how it undermines the arguemnt that 100 years have passed without Applicants discovery being implemented. This is not persuasive because (1) it has not been 100 years since discovery and implementation (see Aman and Anderson of record). The fact that one did not implement Applicants invention does not mean that is was unobvious. The advantages of carrier conjugates was well known in the art and being readily pursued by multiple parties. Applicants argue that it is unreasonalbe to asser the 100 year delay is merely the result of high development and manufacturing costs. This assertion is not the assertion of the examiner but a position articulated by Klein et al. Applicants assert that the manufacturing costs are not significantly different than other vaccines.. this is again not prsuasive in view of Klein et al. Applicants argue that Merck does not teach a multivalent vaccine employing multiple different carrier proteins… this is quite obvious or the rejection would have been made under 102(b). The rejeciton is a combination of references and the rejection provided proper motivation. Applicants admitt that the art combined different carriers and different polysaccharides but such was not done for pneumonococcal polysaccharides. This is not persuasvive because the fact that it was not done for pneumonococcal polysaccharides does not mean that it was not obvious to do so in view of the suceess of combining different carriers and different polysaccharides in the art. Additionally, it is noted that the skilled artisan could clearly make such compositions and the making of such compositions is clearly not undue. Applicants admitt that the chemistry is known and that the argued vaccine use is not present in all the claims.

The art rejections are maintained for all reasons made of record.

With respect to the 112, first paragraph rejection Applicants argue page 8, lines 12-21. This is not persuasive because it discloses the maximum of Dt and Tt per dose. Applicants argue page 8 in combination with the paragraph bridging page 11-12 that discuss administration of one or several dosages and that dose may be in a volume of 0.1 to 2 mil and this would convey a composition comprising one or more dosages. This is not persuaisve because the liquid unit of a dose does not convey multiple doses in the same vial as is now claimed. The administration of one or more doses does not lead one to a mulit dose single vial as now claimed because applicants are mixing and matching concepts and does not distinguish that the composition in single dose vials. The fact that one or more dosages of vaccine may be needed to vaccinate and individual does not covey a multi-dosage vial as now claimed as opposed to single dosage vials. As such, the mixing of concepts does not provide for conception by way of written description of a multdosage vial composition as claimed. The specificaiton has broad guidelines to composition dose values and does not provoide conception of multidosage composition as is

claimed. Methodology does not provide compositions when the methodology does not indicate the use of a multidosage compostiton. The use of multiple doses can be readily viewed by the skilled atisan to be independent compositions. There is no direction or guidance in the specificaiton to a multidosage composition (i.e. multiple dosages in the same vial). The issue here is multidosage vials.
The rejection is therefore manitained.